Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Currently Amended) A recombinant factor VIII comprising an A1 domain that includes a ~~point mutation~~ substitution of a glutamic acid residue at the fourth position of a ~~in or near at least one~~ calcium binding site of the A1 domain, wherein the recombinant factor VIII has a specific activity, as measured in a one-stage clotting assay, that is higher than that of a wild-type factor VIII.

2-3. (Cancelled)

4. (Currently Amended) The recombinant factor VIII according to claim 53 ~~3~~, wherein the substitution ~~at residue 113 of SEQ ID NO:2~~ is selected from the group consisting of alanine, valine, isoleucine, leucine, asparagine, glycine, and methionine ~~E113A, E113V, E113I, E113N, E113L, E113G, and E113M~~.

5. (Currently Amended) The recombinant factor VIII according to claim 53 ~~3~~, wherein the substitution ~~at residue 113 of SEQ ID NO:2~~ is alanine ~~E113A~~.

6. (Original) The recombinant factor VIII according to claim 1, wherein the recombinant factor VIII has a specific activity at least about twice as great as the activity of the wild-type factor VIII.

7-8 (Cancelled)

9. (Previously Presented) The recombinant factor VIII according to claim 1, wherein the recombinant factor VIII is B domainless.

10. (Cancelled)

11. (Withdrawn—Previously Presented) The recombinant factor VIII according to claim 1, wherein the recombinant factor VIII is chimeric and comprises substitution of one or more domains, or one or more amino acids residues of human factor VIII with corresponding domains or amino acids residues from a non-human mammalian factor VIII.

12. (Original) The recombinant factor VIII according to claim 1, wherein the recombinant factor VIII has a circulating half-life value that is equivalent to or greater than that of the wild-type factor VIII.

13. (Original) The recombinant factor VIII according to claim 1, wherein the recombinant factor VIII is substantially pure.

14. (Withdrawn) The recombinant factor VIII according to claim 1 wherein the recombinant factor VIII further comprises modified inactivation cleavage sites.

15. (Withdrawn) The recombinant factor VIII according to claim 1 wherein the recombinant factor VIII further comprises factor IXa and/or factor X binding domains modified to enhance the affinity of the recombinant factor VIII for one or both of factor IXa and factor X.

16. (Withdrawn) The recombinant factor VIII according to claim 1 wherein the recombinant factor VIII further comprises modified sites that enhance secretion in culture.

17. (Withdrawn) The recombinant factor VIII according to claim 1 wherein the recombinant factor VIII further comprises modified serum protein binding sites that enhance the circulating half-life thereof.

18. (Withdrawn) The recombinant factor VIII according to claim 1 wherein the recombinant factor VIII further comprises at least one glycosylation recognition sequence that is effective in decreasing antigenicity and/or immunogenicity thereof.

19. (Original) A pharmaceutical composition comprising the recombinant factor VIII according to claim 1.

20. (Original) The pharmaceutical composition according to claim 19 further comprising a stabilizer.

21. (Original) The pharmaceutical composition according to claim 19 further comprising a delivery vehicle.

22. (Original) The pharmaceutical composition according to claim 19 further comprising a pharmaceutically acceptable carrier.

23-47. (Cancelled)

48. (Withdrawn) A method of treating an animal for hemophilia A, the method comprising:

administering to an animal exhibiting hemophilia A an effective amount of the recombinant factor VIII according to claim 1, whereby the animal exhibits effective blood clotting following vascular injury.

49. (Withdrawn) The method according to claim 48, wherein the effective amount comprises between about 10 to about 50 units/kg body weight of the animal.

50. (Withdrawn) The method according to claim 48 wherein the animal is a mammal.

51. (Withdrawn) The method according to claim 50 wherein the mammal is selected from the group consisting of human, rat, mouse, guinea pig, dog, cat, monkey, chimpanzee, orangutan, cow, horse, sheep, pig, goat, rabbit, and chicken.

52. (Withdrawn) The method according to claim 48 further comprising:
periodically repeating said administering.

53. (Currently Amended) A recombinant factor VIII comprising an A1 domain having a calcium binding site according to one of SEQ ID NOS: 4-7 except that the calcium binding site has a substitution ~~that includes a point mutation~~ of the ~~amino~~ glutamic acid residue at the fourth position thereof ~~corresponding to position 113 of SEQ ID NO: 2~~, wherein the recombinant factor VIII has a specific activity, as measured in a one-stage clotting assay, that is higher than that of a wild-type factor VIII.

54. (New) A recombinant factor VIII comprising an A1 domain, and A2 domain, an A3 domain, a C1 domain, and a C2 domain, wherein the A1 domain comprises a calcium binding site that is homologous to and shares Glu and Asp residues with SEQ ID NO: 3, and which calcium binding site further comprises a substitution of a wild-type Glu residue at the

fourth position of the calcium binding site, wherein the substitution results in a recombinant factor VIII having a specific activity, as measured in a one-stage clotting assay, that is higher than that of a wild-type factor VIII.